"anxiety/depressive state" is found at page 19, lines 28-34; support for the term "obsessive/compulsive behavior" is found at page 19 lines 24-27; and support for the terms "hypertension" and "arrhythmias" is found at page 19, lines 36-37. Support for the phrase "recovering from surgical anesthesia" as a cause of emesis is found at page 18, line 6.

Claims 1-57 are in this application. Claims 1, 40-43, 45 and 52 were rejected under 35 USC § 112, first and second paragraphs. Claims 2-39, 44 and 46-51 were objected to as being dependent upon a rejected base claim. Claims 53-60 were withdrawn from consideration as being claims to subject matter not elected for examination.

Restriction Requirement

In response to a telephonic election of species requirement by Examiner B. Tevardzik, December 12, 1991, the Applicants elected for examination the single disclosed specie of Claim 7, i.e., 2-(1-azabicyclo[2.2.2]oct-3-yl)-1,2,3,5-tetrahydrocyclopent[*de*]isoquinolin-1-one. Claims 1-9 read on the elected species or its individual isomers. The election of species requirement is not incorporated in the Office Action mailed January 28, 1992.

In response to a telephonic restriction requirement on January 9, 1992, The Applicants elected for examination Group I, Claims 1-34, drawn to compounds, pharmaceutical compositions, and the uses thereof. In the formal Restriction Requirement incorporated in the Office Action mailed January 28, 1992, Group IV is defined as containing Claim 57, drawn to intermediates, and Claims 58-60 are not included in any of the defined groups. Because Claims 58-60 are either directly or indirectly dependent from Claim 57, the Applicants assume that the formal Restriction Requirement contains a typographical error and that Group IV includes Claims 57-60 and that Claims 53-60 are withdrawn from consideration. Restriction between Group I and Group II (Claims 53-54, drawn to a process) and Group III (Claims 55-56, drawn to a process) is traversed for the following rationale.

A requirement for restriction between distinct claimed subject matter is proper if reasons are provided to support a conclusion that a serious burden would result were the restriction not required. MPEP § 803. In order to establish reasons for insisting upon the restriction, one of the following

must be shown by appropriate explanation: (1) separate classification, or (2) if classified together, a separate status in the art (i.e., each subject is forms a separate focus for inventive effort), or (3) if classified together, it is necessary to search a field of art in the examination of one subject where no pertinent art to the other exists. MPEP § 808.02. The reason provided for insisting upon the restriction requirement in the present instance is that each group has a separate classification. However, each of Groups I, II and III are classifed in Class 546, subclass 99, 100.

The Applicants contend that because no reasons are offered to show that the concurrent examination of Groups I, II and III will result in a serious burden upon the PTO, insisting upon the restriction requirement is procedurally improper. Accordingly, the Applicants respectfully request that the requirement be withdrawn.

Rejection Under 35 USC § 112

Claims 1 and 40 were rejected under 35 USC § 112, second paragraph for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the descriptions "acyloxy" and "esterified" in Claim 1 are objected to under the rationale that the term acyloxy could include groups derived from phosphonic acid or sulfonic acid and that it is unclear what scope the stem of an acyloxy substituent or an esterifying group of the esterified carboxy substituent would encompass.

Applicants respectfully contend that a claim is not rendered indefinite if one of ordinary skill in the relevant art, having the disclosure and the claim before them, can determine with a reasonable degree of certainty the subject matter encompassed within the claim. The terms objected to are described in the disclosure of the present application. At page 7, line 30, of the application, the term "esterified carboxy" is defined as the ester group -COOR, wherein R is C_{1-8} alkyl. At page 7, line 32, the term "acyloxy" is defined as a group -OC(O)R, wherein R is C_{1-8} alkyl. The definition of the term "alkyl" is set forth at page 7, line 8.

The term "effective" in Claim 40 was also objected to and *In re Fredricksen*, 102 USPQ 35, was cited as support for rejecting the claim. In *In re Fredricksen*, the CCPA supported the assertion that when a specification fails to disclose the metes and bounds of the operative proportions either generally or specifically, such deficiency is not supplied or corrected by the contention that those

skilled in the art would know what the maximum or optimum amounts would be.

In *Ex parte Skuballa*, 12 USPQ2d 1570, the POBAI held that the term "effective amount" is definite and the recitation of an intended use is not required if the specification provides adequate guidelines as to intended utilities and how the uses can be effected. Adequate guidelines include a description that the instant compounds exhibit the properties typical for compounds with similar pharmacology and can be used to achieve similar biological responses. The Applicants submit that *Ex parte Skuballa* is the most recent and relevant decision to the present instance and that both *Ex parte Skuballa* and *In re Fredicksen* stand for the proposition that the term "effective amount" is definite if the specification provides adequate support for such term.

The present application fully describes how to utilize the compositions of Claim 40 (e.g., see therein page 17, line 35, through page 20, line 15) and what a therapeutically effective amount is (e.g., see therein page 22, line 21, through page 24, line 20). Thus, the Applicants contend that one of ordinary skill in the art of treating the diseases for which the compounds of the present invention are useful will, in reliance upon the disclosure of the present application and without extensive experimentation, be able to determine a therapeutically effective amount for a given disease.

Applicants contend that in light of the present application disclosure as interpreted by one of ordinary skill in the art, the claims do particularly point out and distinctly claim the subject matter which is regarded as the invention. Applicants, therefore, request that the rejection of Claims 1 and 40 for indefiniteness with respect to the terms "acyloxy", "esterified" and "effective" be withdrawn.

Claims 41-43 and 45 were rejected under 35 USC § 112, first paragraph as not describing in such full, clear, concise and exact terms the claimed invention as to enable any person skilled in the art to make and use the same. The Applicants submit that Claims 41-43 and 45 as amended are enabling under 35 USC § 112 and are now in condition for allowance for the following reasons.

The terms "CNS disorder", "cardiovascular disorder", "gastrointestinal disorder", and "cognitive disorder" are objected to under the rationale that each embrace contradictory conditions and, therefore, the scope of the claims employing such terms cannot be deemed enabled. The Applicants contend that the compounds of the present invention are 5-HT_3 receptor antagonists (e.g., see page 20, line 24, of the present application) and as such are useful in the treatment of a

variety of gastrointestinal, CNS and cardiovascular disorders, (e.g., see page 2, beginning line 1, of the present application). Specific CNS disorders treatable with the compounds of the present invention include anxiety/depressive states, obsessive/compulsive behavior, cognitive disorders, and psychosis (e.g., see page 19, beginning line 14 of the application). Specific cardiovascular disorders treatable with the compounds of the present invention include hypertension and arrhythmias (e.g., see page 19, beginning line 35, of the present application). In addition, compounds of present invention possess prokinetic activity and are therefore useful in treating a wide variety of gastrointestinal disorders treatable with prokinetic agents (e.g., see page 19, beginning line 31, of the application).

The term "cognitive disorder" is objected to under the rationale that it covers unrelated diseases such as depression, Alzheimer's Disease, psychosis and dyslexia. The Applicants contend that the term "cognitive disorder" as intended by the disclosure of the present application (e.g., see page 19, line 18, therein) and as generally accepted by those skilled in the art, relates to specific disorders of the central nervous system in which cognitive function is affected (i.e., decreased level of consciousness, memory and orientation, concentration, knowledge of general information, intelligence, and insight and judgment).

An underlying brain disorder affecting cognitive function may produce symptoms simulating functional neurotic or psychotic syndromes, but psychiatric disorders such as neuroses or psychoses are not caused by cognitive disorders. On the contrary, neurotic illness is not usually characterized by major alterations in mental function or severe disturbances in cognitive and perceptual loss and while cognitive performance may decrease in psychotic illnesses, the causes of such diseases are not associated with a decrease in cognitive function. Finally, dyslexia is a condition in which an individual is unable to interpret written language and is not a psychiatric or cognitive disorder. Dyslexia is a learning disability which has no basis in cognition or intelligence.

The separate use of the term "emesis" in Claim 41 is objected to under the rationale that it would appear to fall under the category of a gastrointestinal disorder. While emesis is, in general, considered a gastrointestinal disorder, for the purposes of the present application, emesis is defined in a broader sense and includes not only vomiting, but nausea and retching as well (i.e., see page 8, line 29 of the present application). Because of this broad definition of the term emesis and because

the term "gastrointestinal disorder" in Claim 41 is now amended to read "gastrointestinal disorder treatable with prokinetic agents", the Applicants do not consider the use of emesis in Claim 41 as redundant.

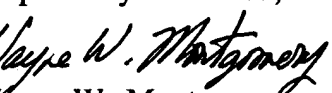
In view of the above amendments and remarks, Applicants request that the rejection of Claims 41-43 and 45 as non-enabling be withdrawn.

CONCLUSION

Applicants respectfully submit that all rejections of the Claims are overcome, and the application is in condition for allowance.

Please correct the eighth reference in the Information Disclosure Statement (i.e., *J. Med. Chem.*, **1990**, *33*, 2942-2944 **(Salituro et al)**) and the corresponding listing on Form PTO-1449 by replacing the authors "Salituro et al." with the authors --King et al.--. It is believed that the copy of King et al. transmitted with the IDS was missing page 2944. A complete copy of King et al. is provide herewith.

Respectfully submitted,



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